REMARKS

Claims 1, 3-18, and 20-30 were pending in the present application prior to this communication. By the present communication, claims 18, 20-28 and 30 have been cancelled without prejudice, and new claims 31-55 have been added to define Applicants' invention with greater particularity. No new matter is introduced by the subject amendments as the new claim language is fully supported by the specification and original claims.

Upon entry of the amendments submitted herewith, claims 1, 3-17, 29, and 31-55 will be pending. The present status of all claims in the application is provided in the Listing of Claims presented herein beginning on page 2 of this communication.

With respect to claim amendments and cancellation, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicants acknowledge with appreciation withdrawal of the §102(e) rejection of claims 1, 6-8 and 29, as asserted in the Office Action mailed on December 6, 2004. Applicants also acknowledge with appreciation withdrawal of the §103(a) rejection of claims 1, 6-8, 18, 20-30 over Grinstaff (U.S. Pat. No. 5,498,421) in view of Westesen, as asserted in the Office Action mailed on December 6, 2004.

Rejection under 35 U.S.C. §112, first paragraph

The rejection of claims 1, 3-18 and 20-30 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement, is respectfully traversed.

Specifically, Applicants respectfully disagree with the Examiner's assertion that the term "non-cancerous cells" is allegedly not supported by the present specification.

It is respectfully submitted that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.'" *Pandroll USA, LP v. AirbossRy. Prods.*, 424 F.3d 1161, 1165, quoting *Union Oil Co. of Cal. v. Atlantic Richfield*, 208 F.3d 989, 997 (Fed. Cir. 2000); *see also Lampi Corp. v. American Power Products, Inc.*, 228 F.3d 1365, 1378 (Fed. Cir. 2000)("[T]he disclosure as originally filed need not provide in haec verba support for the claimed subject matter at issue."). According to the MPEP, an objective standard for determining compliance with the written description requirement is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. MPEP § 2163.02.

It is respectfully submitted that the written description requirement is met by the specification of the instant application. The specification discloses different kinds of hyperplasia or growth of non-cancerous cells. See, e.g., paragraphs [0027] through [0030] (restenosis); paragraph [0031] (stenosis); paragraphs [0033], [0051] and [0058] (neointimal hyperplasia associated with vascular interventional procedures, including angioplasty, stenting, atherectomy, and the like); paragraphs [0039] (neointima formation); and Example 1 (vascular smooth muscle cell proliferation). Given the ample teaching in the present application, one of ordinary skill in the art will readily recognize that Applicants were in possession of the claimed methods of treating hyperplasia or inhibiting growth of non-cancerous cells.

Applicants further note that during an earlier stage of prosecution of the instant application, the Examiner referred to hyperplasia as being abnormal growth of normal cells. For example, in the Office Action dated February 25, 2002, the Examiner states,

> Hunter does not explicitly disclose treating hyperplasia, however hyperplasia, as defined by Dorlands Medical Dictionary, is defined as "the abnormal multiplication or increase in the number of normal cells in normal arrangement in a tissue." As the instant application defines restenosis as "the result of the normal healing response which involves proliferation of smooth muscle cells as well as migration of smooth muscle cells into the area of vascular injury," it is understood by the examiner that restenosis is a species of hyperplasia.

February 25, 2002 Office Action, page 4 (emphasis added).

A similar assertion also appears in a later Office Action. See November 22, 2002 Office Action (citing Dorland's Medical Dictionary definition of "hyperplasia").[1]

Accordingly, Applicants respectfully submit that the specification provides adequate support for "non-cancerous cells" and that one of ordinary skill in the art would understand that Applicants were in possession of the claimed invention as of at least the filing date thereof. Applicants respectfully request withdrawal of the rejection.

Applicants further submit that claim 17 does not contain the term "non-cancerous" and thus should not be subject to this rejection. Furthermore, the term "non-cancerous" in claim 9 is redundant, as it is clear that neointimal hyperplasia associated with vascular interventional procedure refers to growth of non-cancerous cells. Accordingly, claim 9 should not be subject to this rejection.

Applicants further disagree with the Examiner's assertion that the term "amorphous drug" is allegedly not supported by the instant specification. Support for this term can be found throughout PCT/US98/13272 (WO99/00331), from which the instant specification claims priority (and incorporates in its entirety). See, for example, page 27, line 13; page 83, Example 12. A copy of the application is provided herein for the Examiner's convenience (see **Exhibit A**).

---

[1] Most of the medical dictionaries consulted define the term "hyperplasia" similarly. See Dorland's Illustrated Medical Dictionary; Stedman's Medical Dictionary; On-line Medical Dictionary. The Merriam-Webster Dictionary, 10th Edition, however, defines the term "hyperplasia" as "an abnormal or unusual increase in the elements composing a part (as cells composing a tissue)." The Dictionary of Cancer Terms defines "hyperplasia" as "an abnormal increase in the number of cells in an organ or tissue."

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph are respectfully requested.

Rejection under 35 U.S.C. §102(e)

The rejection of claims 18, 20-28, and 30 under 35 U.S.C. §102(e), as allegedly being anticipated by Desai et al. (U.S. Patent No. 5,916,596), is respectfully traversed and has been rendered moot by the cancellation of these claims. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §102(e) are respectfully requested.

Rejections under 35 U.S.C. §103(a)

A. Kunz in view of Westesen

The rejection of claims 1, 3-18 and 20-30 under 35 U.S.C. §103(a), as allegedly being unpatentable over Kunz et al. (U.S. Patent No. 5,733,925) in view of Westesen et al. (U.S. Patent No. 6,197,349), is respectfully traversed. Claims 18, 20-28, and 30 have been cancelled, thus obviating the rejection as to these claims. It is respectfully submitted that this rejection is not applicable to the pending method claims; nor is it applicable to the newly added claims.

Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, three criteria must be met. First, there must be some suggestion, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Third, there must be a reasonable expectation of success. MPEP § 2143. Applicants respectfully submit that, based on the failure to meet one or more of these requirements, a *prima facie* case of obviousness has not been established; therefore, the rejection should be withdrawn.

The methods of the present invention generally entail administering a composition comprising an amorphous drug in nanoparticle form, coated with a protein, wherein said drug is selected from the group consisting of an antineoplastic, an antiproliferative, an angiogenesis

inhibitor, and mixtures of any two or more thereof[2]. The nanoparticles of the present invention, as described in the specification, do not use a polymeric core material to form the matrix of the nanoparticles. See, e.g., page 23, lines 27-30.

Kunz does not teach or suggest such methods. Instead, Kunz discloses use of drug conjugated to a vascular smooth muscle cell binding protein. The microparticulate or nanoparticulate dosage forms disclosed therein, which are directly or indirectly conjugated to vascular smooth muscle cell binding proteins, contain a therapeutic agent dispersed in a polymeric matrix. See, e.g., col. 16, lines 20-40. Although Kunz discloses a ligand-sandwich attachment technique which involves use of "a primary peptide or protein shell," the function of the proteins taught therein is to bring the microparticulate or nanoparticulate dosage form and the vascular smooth muscle cell binding protein together.

Furthermore, with regard to new claims 38, 46 and 54, Kunz neither teaches nor suggests use of albumin in the methods and compositions disclosed therein.

The Examiner's reliance on Westesen in efforts to provide motivation for utilizing amorphous forms of drugs clearly does not cure the deficiencies of Kunz. Furthermore, as explained in the previous response to Office Action, Westesen is directed to particles comprising a supercooled melt of a poorly soluble substance and a stabilizing agent. As readily recognizable by those skilled in the art, particles of supercooled melts are very different in size, shape and composition from the those disclosed in Kunz, or the nanoparticles used in the present invention. Furthermore, to work with melts of a poorly soluble substance, one would, of necessity, have to work at temperatures sufficient to achieve a melt, which elevated temperatures would clearly be incompatible with the function of the protein disclosed in Kunz and the structures of the nanoparticles used in the present invention. As a result, one would not be motivated to combine

[2] Claim 17, for example, recites that the formulation comprises "(i) an amorphous drug in nanoparticle form, wherein said drug inhibits proliferation and cell migration, and (ii) a biocompatible protein, wherein said drug is coated with said protein, and wherein said drug is selected from the group consisting of an antineoplastic, an antiproliferative, an angiogenesis inhibitor, and mixtures of any two or more thereof."

the teachings of Kunz and Westesen to arrive at the methods of the present invention. The obviousness rejection may be properly withdrawn on this ground.

For the same reasons elaborated above, Applicants respectfully submit that there is insufficient basis for reasonable expectation of success. The obviousness rejection may be properly withdrawn on this ground.

Accordingly, Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness. Reconsideration and withdrawal of this rejection under 35 U.S.C. §103(a) are, therefore, respectfully requested.

B. Desai and Kinsella

The rejection of claims 1, 3-17 and 29-30 under 35 U.S.C. §103(a), as allegedly being unpatentable over Desai et al. (U.S. Patent No. 5,916,596) in view of Kinsella et al. (U.S. Patent No. 5,616,608), is respectfully traversed. Similarly, the rejection of claims 1, 3-18 and 20-30 under 35 U.S.C. §103(a), as allegedly being unpatentable over Kinsella et al. in view of Desai et al., is respectfully traversed.

Applicants respectfully submit that Desai et al. is not a proper prior art reference for §103 purposes because of co-ownership. 35 U.S.C. §103(c)(1) provides,

> Subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Applicants respectfully submit that the subject matter disclosed in Desai et al. and the presently claimed invention were, at the time the claimed invention was made, owned or subject to an obligation of assignment to the same entity, namely, American BioScience, Inc. (formerly known as VivoRx Pharmaceuticals, Inc.). Submitted herewith as evidence of co-ownership are recorded assignment documents for Desai et al. (**Exhibit B**) and for the present application (**Exhibit C**). Accordingly, even if Desai et al. qualifies as prior art under §102(e), it cannot be

cited as §103 art. Applicants respectfully request reconsideration and withdrawal of the rejection.

Obviousness-type double patenting

The rejection of claims 18, 20-28, and 30 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-2, 4-6, 13-14, and 17 of U.S. Pat. No. 6,749,868 is respectfully traversed and has been rendered moot by the cancellation of these claims.

The rejection of claims 18 and 20-24 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 22-25 of U.S. Patent No. 6,096,331 in view of Westesen et al. is respectfully traversed and has been rendered moot by the cancellation of these claims.

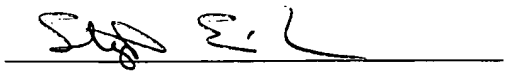
Accordingly, Applicants respectfully request that these rejections be reconsidered and withdrawn.

Conclusion

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date: January 17, 2006

By: 

FOLEY & LARDNER LLP
Customer Number: 30542
Telephone: (858) 847-6711
Facsimile: (858) 792-6773

Stephen E. Reiter
Attorney for Applicants
Registration No. 31,192

Enclosures—Exhibit A—WO99/00331
Exhibit B—Recorded assignment for US Patent No. 5,916,596
Exhibit C—Recorded assignment for the present application